Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/349,479 12/02/94	BORDER	W PLA1245

EXAMINER

HM12/1105

CATHRYN CAMPBELL
CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
SUITE 700
SAN DIEGO CA 92122

ART UNIT	PAPER NUMBER
1644	63

DATE MAILED: 11/05/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 8/30/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 11,12, 21-23, 25 is/are pending in the application.
Of the above, claim(s) 11,12 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 21-23, 25 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 59
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-404-496/40517

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. Applicant's amendment, filed 8/30/99 (Paper No. 62), is acknowledged.
Claim 21 has been amended.

Claims 1-10, 13-20, 24, 26-34 have been canceled previously.

Claims 21-23 and 25 are being acted upon as the elected invention presently.

Claims 11 and 12 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

3. Applicant should amend the first line of the specification to update the status of the priority documents, which are now abandoned.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, including the use of anti-TGF-β antibodies. Applicant should restrict the title to the claimed invention.

5. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 11.

6. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.
Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.
Appropriate corrections are required

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

There is insufficient guidance and direction in the specification as filed to direct the skilled artisan to determine those conditions or pathologies wherein TGF-β production and deleterious accumulation of extracelluar matrix in a tissue exists, commensurate in scope with the claimed invention. Although there appears guidance and direction to glomerulonephritis, ARDS, scarring and liver cirrhosis; applicant has not provided for how the skilled artisan would determine what other pathologies and conditions are a result of existing TGF-β production and deleterious accumulation of extracelluar matrix in a tissue. There appears to be insufficient evidence that applicant's reliance on the either the presence or expression of TGF-β is critical to the deleterious accumulation of extracellular matrix in a wide variety of diseases or in diseases other than those claimed/disclosed in the specification as filed. Although TGF-β may be expressed; there is insufficient objective evidence that TGF-β plays a critical role in the deleterious accumulation of ECM in tissues of a broad range of pathologies and conditions. Also, applicant has not provide sufficient guidance and direction to determine that such deleterious accumulation of ECM exists in various inflammatory conditions. There are distinct differences in the role of inflammatory cytokines such as TGF-β requirements for particular types of inflammation. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, treating pathologies and conditions wherein the deleterious accumulation of ECM in tissues exists would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 21, 23 and 25 are rejected under 35 U.S.C. § 102(e) as being anticipated by Dasch et al. (U.S. Patent No. 5,772, 1998; 1449). Dasch et al. Teaches the use of TGF-β-specific antibodies to neutralize the effects of TGF-β, including lung fibrosis, liver cirrhosis fibrotic skin disorders and scarring (see entire document, including columns 5-6 and the Claims). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993) for the inherency of methods.

12. Claims 21-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dasch et al. (U.S. Patent No. 5,772,998; 1449) in view of Ruoslahti et al. (U.S. Patent No. 5,583,103) AND/OR Bassols et al. (J.Biol. Chem. 263: 3039-3045, 1988; of record, 1449).

Dasch et al. teach the use of TGF-β-specific antibodies to neutralize the effects of TGF-β, including lung fibrosis, liver cirrhosis fibrotic skin disorders and scarring (see entire document, including columns 5-6 and the Claims). Dasch et al. differs from the claimed methods by not disclosing that TGF-β was responsible, at least in part, for glomerulonephritis.

Ruoslahti et al. teach that it was known that excessive accumulation of extracellular matrix in glomerulonephritis was a diseases with a detrimental involvement of TGF-β (see column 2, paragraph 1) and that by treating TGF-β regulated activities, one treats certain pathologies including fibrotic disease and glomerulonephritis (see columns 5-6, overlapping paragraph). Further, Ruoslahti et al. Teach that TGF-β -specific antibodies were able to inhibit the activity of TGF-β (see column 13)

Bassols et al. teach TGF-β regulates the expression of the extracellular matrix chondrotin/dermatan sulfate proteoglycans (see entire document, including Abstract, pages 3041 and 3043). Also, Bassols et al. teach that TGF-β regulates proteoglycans in kidney and lung and that TGFβ induces kidney fibroblast proliferation (see pages 3040-3041).

Given the teachings of Dasch et al. that TGF-β-specific antibodies could neutralize the effects of TGF-β in a several disorders; the one of ordinary skill in the art at the time the invention was made would have motivated to apply such TGF-β-specific antibodies in other disorders where TGF-β- played a role such as glomerulonephritis, as taught and indicated by Ruoslahti et al. and Bassols et al. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Applicant's arguments in conjunction with the Border/Ruoslahti declaration under 37 C.F.R. § 1.131, filed 8/30/99 (Paper Nos. 60/62), have been fully considered but are not found convincing.

First , it is noted that New Grounds of Rejection have been set forth above.

While applicant has provide evidence/Exhibits to indicate prior conception to the prior art as it would read on Dasch et al. (U.S. Patent No. 5,772,998; 1449) above; it does not provide sufficient objective evidence to establish acts in this country commensurate in scope with the claimed invention. For example, development of rabbit anti-TGF-β antiserum (Exhibit A), experiments to characterize the role of TGF-β in experimental models of glomerulonephritis (Exhibit B); a letter between the inventors concerning the role of RGD/PDGF on TGF-β (Exhibit C); sections of a grant Proposal on treating Glomerular disease from January 1989 (Exhibit D) and a draft manuscript subsequent to the Grant Proposal (Exhibit E).

Here, it is noted that the priority date of Dasch et al. (U.S. Patent No. 5,772,998) is December 1988 and that the priority dates of Ruoslahti et al. (U.S. Patent No. 5,583,103) and Bassols et al. (J.Biol. Chem. 263: 3039-3045, 1988) are more than one year prior to applicant's priority date. Therefore, applicant's evidence subsequent to the priority of prior art references is rendered moot.

Applicant's reliance on reagents other than the claimed anti-TGF-β antibodies are not found convincing as supporting the conception, diligence and reduction of practice to the claimed methods of employing said anti-TGF-β antibodies to decrease the deleterious accumulation of extracellular matrix, recited in the instant claims.

With respect to the alleged evidence prior to December 1998; it appears that this evidence is directed toward characterizing the role of TGF-β in certain aspects of glomerular disease and not on the scope of the claimed methods (e.g. methods of decreasing the deleterious accumulation of ECM associated with pathologies and conditions, including ARDS, cirrhosis, scarring). With respect to glomerulonephritis, it does not appear that applicant's evidence supports the use of anti-TGF-β-specific antibodies to inhibit the deleterious accumulation of ECM associated with glomerulonephritis were conceived and reduced to practice previous to the priority dates of the current art rejection under 35 USC 103 set forth above. Also, while applicant has provided notebook pages as evidence of conception, diligence and reduction to practice; these pages together with the comments in the Border/Ruoslahti declaration are not clear on their face. Applicant has the burden to explain the contents of the pages as proof of acts amounting to conception, diligence and reduction to practice. See In re Borkowski and Van Venrooy 184 USPQ 29 (CCPA 1974). Absent a clear explanation of pointing out exactly what facts are established therein and relied upon by applicant, the laboratory notebook pages provide insufficient assistance in enabling the PTO to determine applicant's assertions of conception, diligence and reduction to practice before the prior art as it reads on methods of decreasing the deleterious accumulation of ECM associated with pathologies and conditions, including glomerulonephritis previous to the effective dates of the prior art references.

Applicant's arguments in conjunction with the Border/Ruoslahti declaration under 37 C.F.R. § 1.131 declaration are not found persuasive.

14. The terminal disclaimer filed on 8/20/99 (Paper No. 61), disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of USSNs 08/407,942; 08/459,865; 08/457,707 has been reviewed and is accepted. The terminal disclaimer has been recorded.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Patent Examiner
Technology Center 1600
November 3, 1999

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640